

REMARKS

Applicants now respond to the Office Action mailed May 17, 2005 ("Examiner's Action"). Applicants request reconsideration and withdrawal of all outstanding rejection. A collection of minor amendments have been made to applicants' claimed invention.

As a first matter, Applicant thanks Examiner Mummert and Examiner Fredman for the helpful telephonic interview conducted the morning of Thursday, September 15. During this interview, applicants' Patent Agent (Andy Finn) discussed a distinguishing feature of the presently claimed invention over the Caskey reference. Specifically, applicant pointed out how the final element of claim 1, for example, is not present in the Caskey reference, despite the Examiner's original position that Column 10, lines 63-67 does contain this element of applicants' claimed invention. The Examiner discussed the possibility that labeling each element of applicants' claim 1 with a number, and then explicitly referring back to these numbered elements, might further clarify the distinction between applicants' claimed invention and the Caskey reference. Accordingly, claim 1, claim 16, and newly added claim 21 have been amended to include a number to label each element.

Applicant also discussed the possibility that multiplexation is another distinguishing characteristic of the claimed invention over the Caskey reference. Accordingly, newly added claim 21 addresses this issue.

Finally, the Examiner pointed out that the art contains references by Grossman that might be relevant for the presently claimed invention, and that a pre-emptive discussion of the difference between Grossman and applicants' presently claimed invention might be helpful. Grossman references are cited in the text of the specification of the instant patent application.

For example, the specification cites U.S. Patent 5,514,543 (hereafter, "Grossman"). However, applicants indicated in the telephonic interview, and elaborate further now, that Grossman does not anticipate or make obvious the presently claimed invention. For example, Figure 11A of Grossman shows a PCR comprising a first primer bearing a mobility modifier, and a second primer bearing a label. However, no-where does Grossman teach applicants' presently claimed invention of a first primer comprising both a mobility modifier and a label, and a second primer comprising an affinity moiety. The patentability of applicants' presently claimed invention in light of Grossman, Caskey, and the other references cited by the Examiner in her response dated May 17, 2005, will become clearer still upon consideration of the remainder of this Action.

With respect to claim amendments present in this Action:

a) Claim 1 has been amended with the insertion "first" to more clearly invoke the antecedent basis of this term.

b) Claim 5 has been amended to provide a "different" region of interest. This amendment is provided to more clearly articulate the claimed invention. Support for this amendment can be found, for example, on page 18 lines 10-18.

c) Claim 5 has been amended to more clearly articulate the first primer "of each primer set". This amendment is provided to more clearly articulate the claimed invention in multiplexed embodiments. Support for this amendment can be found, for example, on page 18 lines 10-18.

All of the Amendments discussed in (a-c) are fully supported by the originally filed application. No new matter is introduced by these amendments.

Oath/Declaration

1. Regarding (1) and (2) of the Examiner's Action, applicants note that the inventors indicated on the signed Declaration sent August 27, 2004 are correct. Jeremy Webster was incorrectly listed as an inventor on the originally filed application. Pursuant to CFR §1.48 (f)(1), applicants corrected inventorship with their first submission of the executed Declaration on August 27, 2004.

Specification

2. Regarding (3) of Examiner's Action, applicants agree to remove the browser executable code on pages 1 and 27, consistent with MPEP §608.01.

MPEP §608.01 provides the basis for not permitting an embedded hyperlink and/or other form of browser-executable code in a specification. This section notes that such text in a patent becomes a live web link when it is included in patents posted on the USPTO website. Thus, when a user clicks on such text in the patent on the USPTO website, the user will be transferred to another website which could be a commercial website. USPTO policy does not permit the USPTO to link to any commercial websites.

Accordingly, applicants have amended the URL that was initially filed with the specification by replacing the term "http://www" with the term "world wide web". Thus, although the specification still provides the reader with the information needed to access the website, it no longer includes a link that will permit a user to click on the text of the patent and be transferred to that website. Applicants respectfully request reconsideration and withdrawal of the objection.

35 USC §102

3. Regarding (4-10) of Examiner's Action, applicants make certain amendments to the claims as discussed supra in the interests of expediently advancing prosecution, and for the purposes of more clearly articulating the bounds of applicants' claimed invention. These amendments in no way acquiesce to the Examiner's rejections.

Examiner rejects Claims 1-5, 8-11, 16, and 17 under §102b in view of Caskey, U.S. Patent 5,364,759 (hereafter "Caskey"). In order for a reference to be appropriate for rejection under §102b, the reference must contain each element of applicants' claimed invention. However, a close reading of Caskey illustrates that Caskey fails to teach every element of applicants' claimed invention. Specifically, Caskey fails to teach the following element of applicants' Claim 1:

"releasing the labeled single stranded target polynucleotide from the bound double stranded polynucleotide amplification product by denaturation."

Further, Caskey fails to teach the following element of applicants' Claim 16:

"releasing the labeled single stranded target polynucleotide molecular size standard."

In the Examiner's analysis of this element of applicants' Claim 1 and Claim 16, the Examiner cites Column 10, lines 63-67 of Caskey. These lines read:

"...Fig 2B shows direct DNA sequencing of single stranded template following capture and strand separation of the biotinylated amplification products of λ AE[AGAT]-2 with avidin coated magnetic beads."

A close reading of Caskey indicates that the single stranded template to which the Examiner refers is immobilized on an avidin bead. A sequencing reaction is then performed on this immobilized single stranded template. The resulting sequencing products are presented on the gel images shown in Figure 2B.

However, the invention in Claims 1 and 16 is quite different. Applicants do not necessarily perform a reaction (sequencing, or otherwise) on the immobilized single stranded template. Instead, applicants elute the labeled single stranded target polynucleotide from an immobilized amplicon. This labeled single stranded target polynucleotide was formed in a prior PCR as one of the strands of a resulting amplicon. Applicants' claimed invention then provides for the release of this labeled single stranded target polynucleotide. Applicants' release of their labeled single stranded target polynucleotide is completely different from the teachings contained in Caskey. Caskey only teaches performing a reaction on an immobilized single stranded target, and analyzing the reaction products *that result from* this reaction. Caskey does not teach the direct elution of a labeled single stranded target polynucleotide from a PCR amplicon immobilized on a solid support. Rather, Caskey teaches performing a reaction on the immobilized amplicon, and then subsequently eluting the reaction products *that result from* this reaction.

Thus, claims 1 and 16 of the instant application are novel in view of Caskey.

Applicants further note that claims depending from a novel independent claim are also novel. Thus claims which depend from claim 1 (i.e. claims 2-5 and claims 8-11) are novel, and claims which depend from claim 16 (i.e.-claim 17) are novel. Applicants respectfully request withdrawal of the §102(b) rejection of claims 1-5, 8-11, 16, and 17.

4. Regarding (11-13) of Examiner's Action, Applicants note that the subject claims 18 and 19 have been canceled, thus rendering the Examiner's rejection moot.

35 USC §103

5. Regarding (14-21) of Examiner's Action, the Examiner rejects claims 1-11, and 16-17, under §103(a) as being unpatentable over Caskey in view of Butler, J. Forensic Science, Volume 48 (5), pages 1-11, hereafter "Butler".

In order for a combination of references to support a prima facie obviousness rejection, the references must teach or suggest all the limitation of the claims (see *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970)). However, as discussed supra, Caskey fails to teach the following element of applicants' Claim 1:

"releasing the labeled single stranded target polynucleotide from the bound double stranded polynucleotide amplification product by denaturation."

Further, Caskey fails to teach the following element of applicants' Claim 16:

"releasing the labeled single stranded target polynucleotide molecular size standard."

Butler teaches neither of these elements in applicant's Claim 1 or 16. Thus, neither Caskey, Butler, or the combination of Caskey and Butler, could teach the claimed invention. Applicants further note that claims depending from a non-obvious independent claim are also non-obvious. Thus claims which depend from claim 1 (i.e. Claims 2-11) are novel, and claims which depend from claim 16 (i.e.-Claim 17) are novel. Applicant's respectfully request withdrawal of the §103(a) rejection of Claims 1-11 and 16-17.

6. Regarding (22-23) of Examiner's Action, the Examiner rejects claims 13-15 under §103(a) as being unpatentable over Caskey in view of Coticone, U.S. Patent 6,841,349, hereafter "Coticone".

However, as discussed supra, Caskey fails to teach the following element of applicants' claim 1:

"releasing the labeled single stranded target polynucleotide from the bound double stranded polynucleotide amplification product by denaturation."

Further, Coticone does not teach this element. Thus, neither Caskey, Coticone, or the combination of Caskey and Coticone, teach applicants' claimed invention. Thus, applicant's respectfully request withdrawal of the §103(a) rejection of claims 13-15.

7. Regarding (24-25) of Examiner's Action, the Examiner rejects claims 1,5, and 12 under §103(a) as being unpatentable over Soper U.S. Patent 5,846,727 (hereafter "Soper") in view of O'Neil, U.S. Patent 6,514,699, hereafter "O'Neil".

However, as discussed supra for Caskey, Soper fails to teach the following element of applicants' claim 1:

"releasing the labeled single stranded target polynucleotide from the bound double stranded polynucleotide amplification product by denaturation."

In the Examiner's analysis of this element of Applicants' claims 1, 5, and 12, the Examiner cites Column 5, lines 29-30 of Soper. These lines, with some additional surrounding text included by applicants to provide relevant context, read:

"The capillary tubes have previously been modified with avidin (or alternatively streptavidin), which serves as an anchor to immobilize the biotin-linked double-stranded DNA's. The DNA oligonucleotides are then purified and denatured, and dye-labeled Sanger dideoxy products are produced directly in the tube using solid-surface methods."

Thus, a close reading of Soper indicates that the single stranded template to which the Examiner refers is immobilized on an avidin bead. A sequencing reaction is then performed on this immobilized single stranded template. The resulting sequencing products are then released.

However, Applicants' claimed invention in claim 1, and dependent claims 5 and 12, is quite different. Applicants need not necessarily perform a reaction (sequencing, or otherwise) on the immobilized single stranded template. Instead, applicants elute the labeled single stranded target polynucleotide from an immobilized amplicon. This labeled single stranded target polynucleotide was formed in a prior PCR as one of the strands of a resulting amplicon. Applicants' claimed invention then provides for the release of this labeled single stranded target polynucleotide. Applicants' release of their labeled single stranded target polynucleotide is completely different from the teachings contained in Soper. Soper teaches performing a reaction on an immobilized single stranded target, and analyzing the reaction products *that result from* this reaction. Soper does not teach the direct elution of a labeled single stranded target polynucleotide from a PCR amplicon immobilized on a solid support. Rather, Soper teaches performing a reaction on the immobilized amplicon, and then subsequently eluting the reaction products *that result from* this reaction.

O'Neil does not teach this element of applicants' claimed invention. Thus, neither Soper, O'Neil, or the combination of Soper and O'Neil, teach applicants' claim 1. Since the combination of references fails to teach or suggest all the limitations of the applicant's claim 1, it cannot be appropriately rejected under §103(a). Applicants further note that claims depending from a non-obvious independent claim are also non-obvious. Thus claims which depend from claim 1 (i.e.

claims 5 and 12) are non-obvious. Applicants respectfully request withdrawal of the §103(a) rejection of claims 1, 5, and 12.

8. Regarding (26-29) of Examiner's Action, Applicants note that the subject claims 18 and 19 have been canceled, thus rendering the Examiner's rejection moot.

Conclusion

Applicants respectfully assert that the application is in condition for allowance and request issuance of a Notice of Allowance. If the Examiner does not consider the application to be in condition for allowance, applicants request that she call the undersigned at (650) 554-3392 to set up an interview.

Please grant any extension of time required to enter this response and charge any additional required fee to Deposit Account **01-2213 (Order No. 5135)**.

Respectfully submitted,

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